Lysophosphatidic acid enhances stromal cell-directed angiogenesis.

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Public Summary:
Ischemic diseases such as peripheral vascular disease (PVD) affect more than 15% of the general population and in severe cases result in ulcers, necrosis, and limb loss. While the therapeutic delivery of growth factors to promote angiogenesis has been widely investigated, large-scale implementation is limited by strategies to effectively deliver costly recombinant proteins. Multipotent adipose-derived stromal cells (ASC) and progenitor cells from other tissue compartments secrete bioactive concentrations of angiogenic molecules, making cell-based strategies for in situ delivery of angiogenic cytokines an exciting alternative to the use of recombinant proteins. Here, we show that the phospholipid lysophosphatidic acid (LPA) synergistically improves the proangiogenic effects of ASC in ischemia. We found that LPA upregulates angiogenic growth factor production by ASC under two- and three-dimensional in vitro models of serum deprivation and hypoxia (SD/H), and that these factors significantly enhance endothelial cell migration. The concurrent delivery of LPA and ASC in fibrin gels significantly improves vascularization in a murine critical hindlimb ischemia model compared to LPA or ASC alone, thus exhibiting the translational potential of this method. Furthermore, these results are achieved using an inexpensive lipid molecule, which is orders-of-magnitude less costly than recombinant growth factors that are under investigation for similar use. Our results demonstrate a novel strategy for enhancing cell-based strategies for therapeutic angiogenesis, with significant applications for treating ischemic diseases.

Scientific Abstract:
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